REMARKS

Claims 1, 3, 4, 6, 10-13, 17, 19, 20 and 22-25 are pending and claims 7-9 are withdrawn from consideration. Applicants have amended claims 1, 3, 17, 19, and 25, which amendments do not introduce any new matter.

Priority Date of the Present Application

The Examiner states that the provisional application Serial No. 60/310,196 (the '196 application), to which the present application claims priority, does not appear to provide sufficient written description for the claimed limitations. Applicants respectfully traverse.

Applicants believe that the '196 application provides ample written description for the claimed limitations. For example, Applicants call the Examiner's attention to claim 1 as previously presented, which is directed to a method of reducing a T cell-mediated immune response in an individual diagnosed as having a condition characterized by an excessive or unwanted T cell-mediated immune response by administering to the individual a composition comprising an effective amount of an antibody or antigen-binding fragment thereof that specifically binds to P-Selectin Glycoprotein Ligand-1 (PSGL-1) on the surface of a T cell, wherein the binding of the antibody or antigen-binding fragment thereof to PSGL-1 on the surface of the T cell induces a signal transduction pathway that results in the death of the T cell, thereby reducing a T cell-mediated immune response in the individual. First, Example 9 of the '196 application presents detailed data which have led Applicants to identify TAIP as PSGL-1. Next, the '196 provides detailed description on the making and using of anti-TAIP, i.e., anti-PSGL-1 antibodies, such as for example at pages 8 to 9 of the '196 application (in particular, beginning at the last paragraph on page 9, therapeutic uses of anti-TAIP antibodies are disclosed). The '196 application also describes in detail various conditions that are characterized by an excessive or unwanted T cell-mediated immune response, such as for example at page 15. Moreover, Examples 3 and 6 of the '196 application provide experimental results that demonstrate the ability of an anti-PSGL-1 antibody to induce death of activated T cells in vitro and in vivo. Example 8 of the '196 application further provides an animal model for a condition (transplant rejection) that is characterized by an excessive or unwanted T cell-mediated immune response and related experimental results that demonstrate an anti-PSGL antibody's

effectiveness in ameliorating that condition. Accordingly, the '196 application provides ample written description for each and every limitation of claim 1 as previously presented.

Similarly, all the elements of other pending claims find ample support in the '196 application as filed. To be precise, the present application includes two more Examples (10 and 11). Example 10 is directed to experimental results obtained by an anti-human PSGL-1 antibody, confirming that activated human T cells also undergo apoptosis induced by that antibody. Example 11 is directed to experimental results with an animal model of autoimmune diabetes, another condition characterized by an excessive or unwanted T cell-mediated immune response in the host animal, confirming that an anti-PSGL antibody is effective in the treatment (including prophylactic and therapeutic treatments) of that condition. Relative to the '196 application, Examples 10 and 11 may be characterized as post-filing evidence. With respect to such post-filing date evidence, the Federal Circuit, in *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995), held that such evidence, although not "render[ing] an insufficient disclosure enabling," can be used "to prove that the disclosure was in fact enabling when filed . . . ." As discussed above, the Examples, in particular, Examples 10 and 11, disclosed in the present application that were not in the '196 application are merely to confirm what was already disclosed in the present application as filed, not to add anything new or cure any insufficiency of the '196 application.

Therefore, Applicants submit that the present application is fully entitled to claim priority to and benefit from the filing date of the '196 application, and reconsideration of this issue by the Examination is respectfully requested.

Rejection Under 35 U.S.C. § 112, New Matter

Claims 4 and 20 are rejected under 35 U.S.C. § 112, first paragraph, as "new matter." The Examiner states that the present application only discloses a species, "an anti-hamster Ig" in an Example, to support the claim element of a subgenus of "antibody" that can bind to the anti-PSGL-1 monoclonal antibody and induce the cross-linking of a plurality of PSGL-1 antigens. Applicants respectfully traverse this characterization of the disclosure. First, Applicants draw the Examiner's attention to an anti-mouse Ig in Example 3, which is a cross-linker antibody for the positive control experiment with the monoclonal anti-mouse CD3 antibody. Based on this disclosure, as well as the teaching that an anti-hamster Ig was used by Applicants as a cross-

linker antibody for the experiment with the hamster anti-mouse PSGL-1 antibody, one of ordinary skill in art would immediately recognize that Applicants had possession of the subgenus of cross-linking antibodies. Accordingly, Example 3, together with other teachings of the present application provides ample written description for the subgenus that is now an element of claims 4 and 20. Therefore, Applicants' previous amendment did not introduce any new matter, and reconsideration and withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, Lack of Enablement

Claims 4 and 20 also stand rejected for lack of enablement for the scope of cross-linking "antibody." Applicants respectfully traverse. As discussed above, Applicants provide examples of cross-linking antibodies specific to the primary antibodies involved. Various cross-linking agents including antibodies were known in the art at the effective filing date of this application. For example, the references submitted by Applicants accompanying a Supplemental Information Disclosure Statement enclosed herein demonstrate that, various cross-linking antibodies had been known in the art. As non-limiting examples, Shan et al., Blood (1998) 91:1644-1652, teach the use a goat anti-mouse IgG or Fc receptor-expressing cells to induce cross-linking of CD20 through their interaction with the murine anti-CD20 monoclonal antibody; Beckwith et al., Blood (1996) 88:3502-3507, describe the use of cross-linking agents that include normal rabbit IgG and rabbit anti-human IgM conjugated with acrylamide beads. Accordingly, in view of the teachings of the present application and the state of the prior art, one of ordinary skill in the art can obtain a cross-linking antibody as recited in the claims without undue experimentation. Further, Applicants have made the important discovery that cross-linking of PSGL-1 on the surface of an activated T cell can lead to apoptosis of that T cell. Based on the teachings of the present application, one of ordinary skill in the art can rely on routine experimentation to determine whether an antibody can bind to a primary, anti-PSGL-1 antibody and induce cross-linking of PSGL-1 to achieve the desired effects. Accordingly, Applicants submit that the specification as filed fully enables claims 4 and 20, and reconsideration and withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 102(b)

Claims 1, 3, 6, 10-12, 17, 19 and 22-24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Larsen et al. (U.S. Patent No. 5,840,679).

The Examiner has invited the Applicants to clarify the mechanism of action by which the administration of anti-PSGL-1 antibody can reduce T cell-mediated immune response. First, Applicants have made the important discovery disclosed in the present application that certain anti-PSGL antibodies, in the presence of a cross-linking antibody, can induce apoptosis of activated T cells in vitro. Further, such anti-PSGL antibodies can induce apoptosis of T cells in a host animal in vivo, in the absence of a cross-linking antibody that is exogenous to the host animal. Applicants respectfully submit that knowledge of the mechanism of action underlying the claims inventions is not required for patentability.

Applicants further submit that not all anti-PSGL-1 antibodies can induce T cell apoptosis. For example, Applicants have tested various candidate anti-PSGL antibodies, many of which cannot induce death of activated T cells. Should the Examiner require more detailed description of such tests, Applicants can submit a declaration to that effect.

With respect to Larsen et al., Applicants maintain that it cannot inherently anticipate the claimed inventions. First, inherency is not a matter of probabilities; a rejection based on inherency is appropriate only when the teachings in the art lead inevitably to the claimed subject matter. Under the doctrine of inherency, a patent is invalid based on anticipation even if a prior art reference failed to expressively disclose a feature of the claimed invention, as long as the missing feature is a deliberate or a necessary consequence of what was intended. *See Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1366 (Fed. Cir. 1999) ("Where . . . the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results."). A more recent Federal Circuit decision affirmed that the missing feature did not have to be appreciated in the art, but it must be a necessary consequence of the prior art disclosure. *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003). It has been a long standing position of the courts that a prior *accidental* achievement of a product or process does not constitute inherent anticipation, since an accident gives the public no assurance that others can achieve the same result at a later time. 1

Donald S. Chisum, Chisum on Patents § 3.03 (2004) (summarizing case law on inherent anticipation).

Larsen et al. describe PSGL on endothelial cells and that antibodies against PSGL are used to inhibit P-Selectin-mediated cellular adhesion. Further, Larsen et al. teach the use of PSGL itself or a fragment to treat a number of diseases including autoimmune diseases and diabetes, and possible uses of the anti-PSGL antibodies for inflammatory diseases and certain cancers overexpressing PSGL. Finally, Larsen et al. do not appear to have any examples of anti-PSGL antibodies. Thus, based on Larsen et al., one of ordinary skill in the art would have made anti-PSGL antibodies and attempted to identify those that are effective against for inflammatory diseases and certain cancers overexpressing PSGL. However, the lack of any specific examples of anti-PSGL antibodies and any teachings on how to identify particular anti-PSGL antibodies that may achieve the desirable effects by Larsen et al. makes it impossible to conclude that the cited reference would inevitably or necessarily lead to the claimed inventions in the present application. Accordingly, Larsen et al., at most, present a matter of probabilities, and those features of the claimed inventions that are missing from Larsen et al. be a necessary consequence of their teachings. Therefore, the cited art cannot inherently anticipate the pending claims. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 103(a)

Claims 1, 3, 6, 10-13, 19, 20, 22, 23, 24 and 25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Larsen et al., (U.S. Patent No. 5,840,679) in view of Trembleau et al., (J. Immunol. 163:2960-2968, 1999), Yago et al. (J. Immunol. 161:1140-1145 (1998), Hirata et al., (J. Exp. Med. 192:1669-1675, 2000) and Cobbold et al., (U.S. Patent No. 6,056,956).

As discussed above, Larsen et al. do not teach, expressly or inherently, all elements of the pending claims, and the cited references, individually or in combination, do not make up for that deficiency. Accordingly, the pending claims are patentable over the cited art, and reconsideration and withdrawal of this rejection is respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Please charge any fees or credit any overpayments to our Deposit Account No. 18-1945 from which the undersigned is authorized to draw, under order no. 103305-0001-101.

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Respectfully submitted,

By_____

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